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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/905,508	08/04/1997	LALEH SHAYESTEH	02307O-06772	5513

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TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER 8TH FLOOR
SAN FRANCISCO, CA 941113834

EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	27

DATE MAILED: 04/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/905,508	SHAYESTEH ET AL.	
	Examiner	Art Unit	
	Jehanne E Souaya	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner reviewing your application at the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Jehanne Souaya.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/26/2002 has been entered.

2. Currently, claims 37-39 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Response to Applicant's arguments follow. This action is NON-FINAL.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see for example: p. 7, line 30). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Inventorship

4. The request to correct the inventorship in this nonprovisional application under 37 CFR 1.48(c) requesting addition of an inventor(s) is deficient because:

> An oath or declaration by each actual inventor or inventors listing the entire inventive entity has not been submitted.

37 CFR 1.48(c) states: Correction of inventorship in a patent application, other than a reissue application, pursuant to 35. U.S.C. 116.

> (c) Nonprovisional application —inventors added for claims to previously unclaimed subject matter . If a nonprovisional application discloses unclaimed subject matter by an inventor or inventors not named in the application, the application may be amended to add claims to the subject matter and name the correct inventors for the application. If the application is involved in an interference, the amendment must comply with the requirements of this section and must be accompanied by a motion under § 1.634. Amendment of the inventorship requires:
>
> (1) A request to correct the inventorship that sets forth the desired inventorship change;
> (2) A statement from each person being added as an inventor that the addition is necessitated by amendment of the claims and that the inventorship error occurred without deceptive intention on his or her part;
> **(3) An oath or declaration by the actual inventors as required by § 1.63 or as permitted by § § 1.42, 1.43, or § 1.47;**
> (4) The processing fee set forth in § 1.17(i); and
> (5) If an assignment has been executed by any of the original named inventors, the written consent of the assignee (see § 3.73(b) of this chapter)

The request filed February 3, 2003 only contains an executed declaration by two of the inventors. No statement or explanation has been given as to why all of the inventors have not executed the declaration and therefore the request does not comply with 37 CFR 1.48(c) section 3.

Claim Rejections - 35 USC § 112

Enablement

5. Claims 37-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the pathological proliferation of ovarian cancer cells in a patient that has a population of ovarian cancer cells comprising cancer cells in which 3q26.3 is amplified, the method comprising administering a therapeutically effective dose of LY294002 and thereby inhibiting the pathological proliferation of ovarian cancer cells in a patient, does not reasonably provide enablement for a method of inhibiting the pathological proliferation of ovarian cancer cells in a patient that has a population of ovarian cancer cells comprising cells in which 3q26 is amplified, the method comprising administering a therapeutically effective dose of any inhibitor or any non peptidic inhibitor of any PI kinase, wherein the inhibitor inhibits any PI kinase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of inhibiting the pathological proliferation of ovarian cancer cells in a patient that has a population of ovarian cancer cells comprising cells in which 3q26 is amplified, the method comprising administering a therapeutically effective dose of any inhibitor or any non peptidic inhibitor of any PI kinase, wherein the inhibitor inhibits any PI kinase activity. The claims are further drawn to administering the non peptidic inhibitor LY294002. The specification only delineates 3q26.3 as the critical region where increases in copy number are associated with ovarian tumor samples. 3q26, however, defines a much larger region, containing unknown and uncharacterized genes in which an increase in copy number may

or may not be correlated with ovarian cancer. The art does not support a correlation with an increase in copy number in this large region and ovarian cancer. The claims are not drawn to any particular PI kinases, and it is unknown if another PI kinase might be found within this larger region. While the specification and the art of Hu et al (Clinical Cancer Research, 2000; vol. 6, pp 880-886) support the inhibition of ovarian cancer cell proliferation by administering LY294002, the art does not support that PI kinases necessarily have identical activity or function, for example Bonjouklian et al (US Patent 5,378,725) teach that PI-4 kinase phosphorylates PI (phosphatidylinositol), while PI 3 kinase not only phosphorylates PI, but also phosphorylates phosphatidylinositol 4 phosphate (see col. 1, lines 37-56). Further, Bonjouklian et al teach that PI 3 kinase inhibitors described in the patent do not inhibit PI 4 kinase activity. Therefore, without a correlation as to the structure of LY294002 and its function as a PI 3 kinase inhibitor, that is, which function of PI 3 kinase does it inhibit and how, no predictable correlation can be made as to the structure of general PI kinase inhibitors, general PI 3 kinase inhibitors, or that because LY294002 inhibits PI 3 kinase activity, it necessarily inhibits any PI kinase.

The specification teaches that ovarian cancer cell lines and ovarian tumor cells exhibited an increase in copy number of 3q26.3 (p. 28). The specification teaches that the gene encoding the catalytic polypeptide of PI3 kinase (PIK3CA) is found within this region (see p. 29). The specification teaches that PI3 kinase activity is increased in cells that have an increase in copy number of PIK3CA (pp 32-33). The specification teaches ovarian cancer cell proliferation was inhibited in vitro by administering LY294002 (p. 32), a PI 3 kinase inhibitor, to cells with increased copy number of PIK3CA. The art of Hu et al provides corroborative evidence that ovarian cancer cell proliferation is inhibited in vivo by administering LY294002. Hu et al teach

that LY294002, a flavenoid derivative, is a PI 3 kinase inhibitor. Hu et al teach that LY294002 is a specific competitive and reversible inhibitor which can bind and be released from the ATP binding site. However neither the specification nor Hu et al provide any correlation as to the structure of LY294002 and how PI 3 kinase activity inhibition leads to inhibition of ovarian cancer cell proliferation such that the skilled artisan would be able to envision what constitutes a PI 3 kinase inhibitor or a PI 3 kinase inhibitor that would also inhibit the pathological proliferation of ovarian cancer cells. Further, the specification teaches that the mechanism of signal transduction for PI 3 kinase is not completely known (p. 10). Fry teaches (Breast Cancer Research; 2001, vol. 3, pp 304-312) that PI3 kinase was first identified as a lipid kinase (see abstract) and that the PI 3 kinase family has grown to include 12 enzymes, but that some of these have protein kinase activity but not lipid kinase activity. Fry further teaches that although wortmannin has been shown to have anti tumor activity in vitro and in vivo, these effects do not correlate well with inhibition of PI 3 activity (see p. 310, col. 2, lines 12-16 of last para). Therefore, given that the specification teaches that the mechanism of PI 3 kinase signal transduction is not completely known, that the art teaches that different 'activities" can be associated with PI kinases and even PI 3 kinases in general, that the specification does not teach how LY294002 functions to inhibit PI 3 kinase activity, or which PI 3 kinase 'function' it inhibits, that the art teaches that the effect of a known PI 3 kinase inhibitor (wortmannin) which has anti tumor activity both in vitro and in vivo does not correlate well with inhibition of PI 3 kinase activity, and that the art does not teach any correlation as to the structure of LY294002 and how PI 3 kinase activity inhibition leads to inhibition of ovarian cancer cell proliferation, the skilled artisan would not be able to establish a predictable correlation between the structure

of LY294002 and any PI kinase or any PI 3 kinase inhibitor or one that would inhibit the pathological proliferation of ovarian cancer cells.

While the specification teaches examples of known PI 3 kinase inhibitors, such as wortmannin, no correlation is provided between the structures of such and the ability to inhibit PI 3 kinase activity such that the skilled artisan could be able to predictably envision what constitutes a PI 3 kinase inhibitor in general, or one that would function in the claimed method. Further, Bonjouklian teaches that wortmannin and certain analogs of such inhibit PI 3 kinase activity but do not inhibit PI 4 kinase (see col. 10, lines 17-20). It is noted that claim 39 is broadly drawn to using LY29004 to inhibit any PI kinase activity in a method of inhibiting ovarian cancer cell proliferation. However, as exhibited by the teachings of Bonjouklian et al, inhibitors of PI kinases can be specific to a certain PI kinase, and do not necessarily inhibit the class as a whole. Further, Bonjouklian et al do not teach any predictable structure/function correlation between the analogs taught in the patent and therefore do not make up for the deficiencies in the specification as to a predictable correlation between LY294002 and PI 3kinase or general PI kinase inhibiting activity. Given the lack of guidance in the specification as to a predictable structure /function correlation with regard to LY294002 and other PI 3kinase inhibitors, and the unpredictability taught in the art, the skilled artisan would be required to perform extensive trial and error analysis to be able to practice the invention as broadly as it is claimed.

In addition, the teachings in the specification do not support the use of PI kinase inhibitors in general for inhibiting the proliferation of ovarian cancer cells because neither the specification nor the art support a correlation between the generic inhibition of PI kinase activity

and inhibition of ovarian cancer cell proliferation. Other inhibitors which are encompassed by the claims 37 and 38 include compounds which would effect the activity of phosphorylating a substrate by binding to a different sit on the enzyme or which permanently inactivate the enzyme. However, Hu et al teach that LY294002 is a competitive and reversible inhibitor which can bind and be released from the ATP binding site. The specification has not provided guidance to the skilled artisan to determine the structural features of PI kinase inhibitors in general which result in inhibiting any PI kinase activity and also inhibit proliferation of ovarian cancer cells. The specification has not taught that generally inhibiting any PI kinase also results in inhibition of ovarian cancer cell proliferation.

Further, the recitation of "inhibitor of PI kinase... wherein the inhibitor inhibits PI kinase enzymatic activity" encompasses methods of inhibiting expression of PI kinase using nucleic acids in gene therapy. The specification, however has not provided any teachings or demonstrations that inhibition of ovarian cancer cell proliferation can be achieved using any of these potential inhibitors. It is further noted that at the time of filing, gene therapy of disease was considered an unpredictable art. Verma et al. teaches that," ... the lack of efficient delivery systems, lack of sustained expression, and host immune reactions - remain formidable challenges" in gene therapy, and specifically identifies the "Achilles heel" of gene therapy as gene delivery (Verma et al. (1997) Nature, Vol. 389, page 239, column 1, paragraph 1, and column 3, paragraph 2). In particular, Verma points out that, " [a] critical limitation of retroviral vectors is their inability to infect non-dividing cells, such as those that make up muscle, brain, lung, and liver tissue " (page 240, column 1, paragraph 3). Verma also teaches that the choice of an appropriate enhancer-promoter combination is critical to the level and consistency of gene

expression from a particular vector and that , " .. the search for such combinations is a case of trial and error for a given type of cell" (page 240, column 2, paragraph 2, and column 3, line 1). Orkin et al. concurs, stating that, "[m]ajor difficulties at the basic level include shortcomings in all current gene transfer vectors and an inadequate understanding of the biological interaction of these vectors with the host", and that "[w]hile the expectations and the promise of gene therapy are great, clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol.." (Orkin et al. (1995) Report to the NIH, page 1, paragraphs 3-4).

Written Description

6. Claims 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The essential feature of the claimed invention is the correlation between inhibition of PI 3 kinase activity in cells and the resulting inhibition of proliferation of ovarian cancer cells in vitro by administration of LY294002. The claims, however, encompass administering a large genus of inhibitors of any PI kinase. The single disclosed species of LY294002 is not representative of the large genus of inhibitors encompassed by the claims. Inhibitors which are encompassed by the claims include nucleic acids for gene therapy, antisense nucleic acids, ribozymes, antibodies, peptides, and non-peptidic compounds such as wortmannin and LY294002. This genus includes structurally and functionally different compounds. However, LY294002 is not considered to represent a substantial portion of the claimed genus. The specification does not describe any

common structural feature of a PI kinase inhibitory compound or a PI 3 kinase inhibitory compound such that the skilled artisan would be able to envision what constitutes a PI kinase inhibitor or a PI 3 kinase inhibitor. No structure/function correlation can be made with regard to LY294002 and nucleic acids, ribozymes, antibodies, peptides or non peptidic inhibitors in general and inhibition of proliferation of ovarian cancer cells. The specification provides no demonstration or guidance that any of these potential inhibitors actually inhibited the pathological proliferation of ovarian cancer cells in a population of cancer cells with an increased copy number of 3q26 or even 3q26.3. With regard to claim 38, while the specification asserts wortmannin and rapamycin (see p. 24) as examples of non peptidic inhibitors of PIK3CA activity, neither the specification nor the reference of Bonjouklian et al teach how wortmannin or analogs of such, for example, act to inhibit PI 3 kinase activity. Hu et al teach that LY294002 is a competitive and reversible inhibitor which can bind and be released from the ATP binding site, however, neither the specification nor the art teach how LY294002 acts to inhibit PI 3 kinase activity such that ovarian cancer cell proliferation is inhibited. Accordingly, no comparison can be made with regard to the structures of the disclosed inhibitors and the function of inhibition of PI 3 kinase activity or inhibition of ovarian cancer cell proliferation through inhibition of PI 3 kinase. Without a disclosure of such, the skilled artisan would not be able to envision what constitutes a PI kinase inhibitor or a PI 3 kinase inhibitor that would function in the claimed method. For example, Boytim et al teach (Journal of Clinical Investigation, vol. 105 pp 1447-1453; 2000) of a synthetic peptide termed DQ 65-79 (corresponding to residues 65-79) of DQA*03011) which inhibited PI 3 kinase in vitro. This inhibitor is structurally very different from that of LY 294002, however, the specification does not provide enough guidance or

description such that the skilled artisan would have been able to envision the structure of DQ 65-79 as a PI 3 kinase inhibitor or would have been able to predict that DQ 65-79 was a PI kinase inhibitor based on its structure. It is further noted that wortmannin and the analogs disclosed in the Bonjouklian patent, as well as rapamycin are not representative of inhibitors of any PI kinase (as encompassed by the claims), as Bonjouklian teaches that while these compounds inhibited PI 3 kinase, they did NOT inhibit PI 4 kinase (see paragraph bridging columns 12 and 13). Bonjouklian et al teach that wortmannin and the analogs disclosed were *selective* PI 3 kinase inhibitors. With regard to the disclosure in the specification of rapamycin as an inhibitor, the art does not support the assertion that rapamycin is a PI 3 kinase inhibitor. Boytim et al teach that rapamycin did not inhibit PI 3 kinase activity in vitro (see abstract). With regard to claim 39, the specification and the art of Hu et al teach inhibition of proliferation of ovarian cancer cells by LY294002 targeted PI 3 kinase. The specification provides no description or guidance that LY294002 inhibited the proliferation of ovarian cancer cells by targeting PI kinases in general or PI kinase activity in general.

The genus of PI kinase inhibitors and PI 3kinase inhibitors appears to be diverse as exemplified by the art cited above. Additionally, Minaguchi et al (Cancer Research, 1999, vol. 59, 6063-6067) teach that PTEN gene product encodes a phosphatidylinositol phosphate which antagonizes the PI kinase mediated pathway and suggests that overexpression of this gene product could be effective as a therapy for ovarian cancer by inhibiting PI kinase activity. Again, this inhibitor is structurally very different from that of LY294002 or wortmannin or rapamycin. The specification does not describe such an inhibitor of PI kinases, yet the inhibitor of Minaguchi et al would be encompassed by the claims as written.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of LY294002, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and *by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.*" Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Response to Arguments

7. The response traverses both rejections (enablement and written description; outlined in sections 5 and 6 above, respectively) under 35 USC 112/first paragraph. The response asserts that the current invention is not a genus of PI 3 kinase inhibitors and that PI 3 kinase inhibitors

are well known, such as those described in the specification at page 24, lines 7-10. The response further cites the MPEP and states that PI 3 kinase inhibitors have been extensively studied and thus the state of the art is advanced. The response concludes that therefore, the specification, taken together with that which is known in the art, provides sufficient description and guidance for the skilled artisan to identify PI kinase inhibitors that inhibit the pathological proliferation of ovarian cancer cells. This argument has been thoroughly reviewed but was not found persuasive. Firstly, as stated in the rejections in sections 5 and 6 above, PI 3 kinase inhibitors do not necessarily inhibit all PI kinases. The claims are directed to generally inhibiting PI kinases, however, the art of Hu et al teach that LY294002 is a PI 3 kinase and Bonjouklian et al teach that wortmannin and analogs of such are selective PI 3 kinase inhibitors. These compounds are not representative of PI kinase inhibitors in general. Further, although the specification asserts that rapamycin is a PIK3CA inhibitor, Boytim et al teach that rapamycin did not inhibit PI 3 kinase activity in vitro (see abstract). While PI 3 kinases have been studied, the art is not so advanced that the skilled artisan, reading the instant specification would have been able to determine that specification had provided a description of the PI kinase inhibitor PTEN gene product taught by Minaguchi et al or the PI 3 kinase inhibitor DQ 65-79 taught by Boytim or that the specification had provided enough guidance that the skilled artisan would have been able to predict their structure or function. While the instant claims are drawn to methods, the methods encompass a large genus of compounds that have not been described. Further, the specification provides no predictable correlation as to the structure of the disclosed PI 3 kinase inhibitors and the function of inhibition of ovarian cancer cell proliferation such that the skilled artisan could envision the

structure of compounds or molecules that would be encompassed by the broadly claimed invention.

The response further asserts that the rejections appear to be concerned that the specification does not provide a description of compounds that inhibit ovarian cancer cell growth without causing potential side effects on non cancerous cells. This argument is considered moot as neither the previous office action nor the present office action required any description of safety or a showing of potential side effects.

The Declaration by Joe Gray has been thoroughly reviewed and was found persuasive with regard to the following: a method of inhibiting the pathological proliferation of ovarian cancer cells in a patient that has a population of ovarian cancer cells comprising cancer cells in which 3q26.3 is amplified, the method comprising administering a therapeutically effective dose of LY294002 and thereby inhibiting the pathological proliferation of ovarian cancer cells in a patient. As the claims are not drawn to such, the claims have been rejected for the reasons set forth above and in previous office actions.

New Matter

8. Claims 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The claims have been amended to recite "cells in which 3q26 is amplified". This amendment appears to be drawn to the amplification or increased copy number of the complete region of 3q26, however the

specification does not appear to teach or provide support for any ovarian cancer cells in which all of 3q26 is amplified. At page 33, lines 1-3, the specification states "cancer cell lines and tumors showing increased PIK3CA copy number". Further, the specification teaches that the critical region exhibiting increased copy number to be that of 3q26.3. However, the 3q26 region is much larger. Additionally, the originally filed claims were limited to 3q26.3 (32) and also do not support the larger 3q26 region.

Indefinite

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 37-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is indefinite in the recitation of "comprising cells" as there is insufficient antecedent basis for the term "cells". It is unclear if this term refers to cancer cells or normal cells. Claim 37 is further indefinite as it is unclear if the recitation of "3q26 is amplified" encompass a region within 3q26 or all of 3q26. The specification does not support a correlation between ovarian cancer cells and an increase in copy number of the complete region of 3q26. The specification only teaches delineating the critical copy number increase region to be 3q26.3.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(f) he did not himself invent the subject matter sought to be patented.

12. Claims 37 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonjouklian et al (US Patent 5,378,725; 1/3/1995).

Bonjouklian et al teach (and claim) a method of treating neoplasms in mammals by administering non peptidic inhibitors (see col. 3, col. 4, table 1; col. 6, lines 49-60; and claims 1-9). Bonjouklian et al specifically teach a method for treating a phosphatidylinositol 3 kinase dependent condition in a mammal, such as abnormal cell growth as found in neoplasms, such as ovarian cancer, by administering a phosphatidylinositol 3 kinase inhibiting amount of a compound as shown in cols 2, 3, and 4 (col. 6, lines 49-col. 7, line 2). Bonjouklian et al teach how to determine quantity of compound to produce a desired therapeutic effect (col. Lines 54-62). It is noted that Bonjouklian et al do not teach "population of ovarian cancer cells comprising cells in which 3q26 is amplified", however such is considered an inherent property of ovarian cancer as exemplified by the teachings in the specification (see p. 28, lines 22-24) "all paraffin embedded ovarian tumor samples also show the same region of increase in copy [n]umber that were seen in the ovarian cancer cell lines". Further, this is exemplified by Sonoda et al (Genes, Chromosomes, and Cancer; vol. 20, pp 320-328, 1997) which teach that in ovarian carcinomas, the most frequent sites of amplification included 3q26.3 (see abstract).

13. Claims 37-39 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Applicants filed a request under 37 CFR 1.48(c) to add an inventor as the claims were amended to add subject matter which required an additional inventor. The

request was found deficient for the reasons set forth above (see section 4). Accordingly, the inventorship has not been changed. Given applicants' statement that the subject matter claimed was not invented by the present inventive entity, the claims are rejected under 35 USC 102(f). This rejection can be overcome by a complete filing as required by 37 CFR 1.48(c).

Conclusion

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
3/27/03